

22nd July 1955

THE MAJOR REQUIREMENTS OF THE A.R.C. RESEARCH GROUP

During the past six months substantial progress has been made in our studies of the structure of tobacco mosaic virus. The work has reached a stage at which we can feel confident that given greater facilities we could advance much more quickly, both as regards detailed knowledge of tobacco mosaic virus and a better general knowledge of the nature of other viruses. Below are listed our principal immediate needs, as well as some suggestions for the future:

1. A Spinco centrifuge. Price £2,400 approx.
2. A second X-ray tube. Price £1,200 approx.
3. Geiger counter spectrometer. Estimated cost approx. £1,500.
4. A biochemist to work full-time for the group in a biochemical laboratory outside this department.

Estimated annual cost £3,000-£5,000 for the first year (depending on what facilities are already available) and subsequently £2,000-£3,000. annually.

5. Starting October 1956, one more crystallographic research worker and one more technical assistant.
6. Additional working space.

1. The Spinco Centrifuge

The need for the Spinco centrifuge has already been described in detail (see attached report) and remains urgent. In order to fulfil the purpose for which we require it, it must be situated in the Crystallography Laboratory.

2. The X-ray Tube

A second X-ray tube is required for immediate use. A new

X-ray camera, made in our own workshop, is now nearly ready, and no tube is available with which it can be used.

The tube which we require is the new Hilger modification of the Ehrenberg-Spear fine-focus tube. One such tube of the batch at present in production has been provisionally reserved for us by Messrs. Hilger and Watts. If ordered in September, this tube would be delivered in October. If our order cannot be placed in September the tube will be sold elsewhere, and we shall have to wait about 12 months for a tube from the next production batch.

3. The Geiger counter Spectrometer.

The photographic method of recording and evaluating X-ray diffraction phenomena is valuable for carrying out a general survey in any given field. It enables a complete diffraction pattern to be surveyed at one glance, and is useful for the rapid measurement of continuous scattering curves when a very high degree of accuracy is not required. It fails, however, in two important respects. Firstly, intensity measurements of very high accuracy cannot be obtained, mainly owing to the non-uniformity and non-reproducibility of photographic film. Secondly, measurements of intensity of scattering at very low angles are extremely inaccurate if the intensity varies rapidly with the angle. Our studies of the structure of tobacco mosaic virus have now reached a stage at which both high-accuracy intensity measurements and very low angle measurements are of critical importance.

Low-angle measurements of diffraction by virus solutions are necessary in order to obtain on an absolute scale the mean

density of the virus as a function of the radius. This is an important aid to the determination of the structure of both the protein and the nucleic acid parts of the virus.

Accurate measurements of intensity at higher angles are necessary when using heavy-atom derivatives of viruses. Recent work in Cambridge has shown that the study of heavy-atom derivatives of proteins makes possible a big advance in our knowledge of protein structures. Heavy-atom derivatives of tobacco mosaic virus (using iodine and mercury) have already been prepared at Berkeley and received by us, and it is probable that a wide range of such derivatives will be prepared in the future. If accurate intensity measurements can be made for both the un-treated virus and its heavy-atom derivatives, it may be possible, in spite of the relatively large size of the virus particle, to investigate the structure of the virus protein in as great detail as that of crystalline proteins such as haemoglobin or ribonuclease. For this purpose it is essential to work with a Geiger counter spectrometer.

4. The Biochemist

We are, at present, entirely dependent on the kindness and goodwill of research workers overseas for our supplies of virus material. We have no regular arrangement, but interesting materials from one German and four American laboratories have been received and studied. One sample of normal tobacco mosaic virus was also prepared for us by Mr. Pirie, but it has not proved possible to obtain any other virus material suitable for our work from laboratories in this country.

While we greatly appreciate the help which we have received

from the American and German laboratories, it is obviously unsatisfactory that we should remain entirely dependent on products prepared, for the greater part, some 6,000 miles away. Nor can we be sure that these laboratories will keep us permanently supplied with material for our research; they may well become interested in other fields in which we cannot collaborate, or they may even set up their own X-ray diffraction laboratories. It is therefore essential that a biochemist should be engaged to prepare virus material for us.

The biochemist should be of Ph.D. standard in order to be capable not only of purifying normal virus material but also of preparing the special derivatives which are required for X-ray structure analysis. The preparation of these derivatives (heavy-atom derivatives, and nucleic acid-free virus protein) requires more skill than the purification of virus.

There is neither space nor facilities for the biochemist to work in Birkbeck College. It seems that the most satisfactory arrangement would be for him to work in one of the A.R.C.'s research establishments in Cambridge, where he would benefit from the proximity of many research workers interested in the structure of plant viruses (in the Molteno Institute and in the Cavendish Laboratory M.R.C. Unit).

The preparation of virus and virus derivatives for our structural investigations would be a full-time job for the biochemist.

5. Increase of Personnel

Dr. A. Klug, Nuffield Fellow in the Birkbeck College Crystallography Laboratory, is interested in the structure of plant viruses and, in collaboration with the A.R.C. group, has already made a substantial contribution to the subject. His tenure of the Nuffield Fellowship ends on 30th September, 1956. In order that his work with the A.R.C. group may continue it is desirable that he be employed as a member of the group as from that date.

In transferring to the A.R.C. group, Dr. Klug would lose the services of his technical assistant. An additional technical assistant would therefore be required at that stage.

6. Working Space

The whole research programme is already severely hampered by excessively cramped working conditions, and this problem will become progressively more acute as the work develops. The work would benefit very greatly if more space could be found near enough to the Crystallography Laboratory to make it possible to expand the existing facilities without losing all the advantages which come to us as a result of being close to and part of Birkbeck College.

Note 1. This report is concerned solely with our major requirements. The present A.R.C. grant for Capital equipment has not been fully spent, but it is not large enough for any one of the items mentioned here. Smaller items, which it is our intention to

purchase out of the existing grant, are not discussed in this report.

Note 2. The success of our work during the past 6 months has been, to a very large extent, a direct result of my visit to America last summer. It is essential to keep in touch with the principal virus research laboratories in America and it will therefore be desirable to re-visit these laboratories within the next year or two. If funds for this purpose are not forthcoming from other sources, a special request will be made to the A.R.C. at a later date.

Rosalind E. Franklin.

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